

group are not only analytically useful in distinguishing closely related compounds but reflect molecular interactions of general importance, as illustrated later by the neutralization behavior of alpha mercapto esters.

Conversion of methyl 2- or 9(10)-mercaptostearate to the corresponding disulfide leaves the infrared spectrum essentially unchanged except for the disappearance of the small 2560 cm^{-1} SH band. Since the irregular methyl ester bands are noted for an α -disulfide, dimethyl 2,2'-dithiodistearate, as well as in the parent mercapto ester, the shifts are not based merely on interaction with the SH group. This conclusion is supported by the fact that the SH frequency is the same within our experimental precision in methyl 2-mercaptostearate as in the 9(10)-compound.

As a further illustration of the interaction of the carbomethoxy groups with alpha substituents, a comparison was made between two hydroxy analogs of the mercapto esters. The spectra of these compounds were measured in carbon disulfide solution because they are solids. Also, the solution spectra avoid complications in the interpretation of intermolecular hydrogen bonding.¹¹

The spectrum of methyl 12-hydroxystearate (Fig. 1C) where the hydroxyl group is remote from the carbomethoxy group, is entirely regular in the $1400\text{--}1150\text{ cm}^{-1}$ region containing the aliphatic methyl and the methyl ester absorptions. It is very similar in this region to methyl 9(10)-mercaptostearate (Fig. 1A) or to methyl stearate.¹¹ Published spectra of somewhat lower resolution show that the spectrum of methyl 12-hydroxystearate is also similar to that of methyl 10-hydroxystearate, an even closer analog to methyl 9(10)-mercaptostearate.¹⁴

With methyl 2-hydroxystearate (Fig. 1D), however, there is a very striking change in the pattern of absorption in the $1400\text{--}1150\text{ cm}^{-1}$ region. It is found, moreover, that the hydroxyl group absorptions differ in the two compounds. The OH stretch is a sharp band at about 3650 cm^{-1} in the methyl 12-hydroxystearate, indicating a free hydroxyl group. In the α -hydroxy compound however, the band is at approximately 3560 cm^{-1} and of greater intensity but still sharp, suggesting intramolecular hydrogen bonding. Weak bonding between the α -hydroxyl group and the carbonyl oxygen atom seems reasonable since it involves a five membered ring.^{14a} Pronounced changes are also observed in the $1150\text{--}1000\text{ cm}^{-1}$ region. These changes probably include a shift in position and intensity of the C—OH stretching vibration in the case of methyl 2-hydroxystearate. The changes in hydroxyl group absorptions, in contrast to the

negligible change in the mercapto group absorptions, support other data showing that hydroxyl groups form hydrogen bonds much more readily than mercapto groups do.¹⁵

Acidity. Evidence for group interactions has also been obtained from titration data on the mercapto compounds. In a chain substituted methyl ester the mercapto group is acidic only when it is in the α -position. When the mercapto group is separated from the ester group, as in methyl 9(10)-mercaptostearate or methyl 11-mercapto-undecanoate, there is no significant uptake of aqueous sodium hydroxide when an alcoholic solution of the ester is titrated to the phenolphthalein end point at room temperature (the usual procedure for determining neutralization equivalents of long-chain carboxylic acids). Methyl 2-mercaptostearate, on the other hand, titrates more like a weak acid. Neutralization to the phenolphthalein end point requires almost an equimolar amount of sodium hydroxide.

A variety of data support the interpretation that the uptake of sodium hydroxide by methyl 2-mercaptostearate involves neutralization of an acidic mercapto group. The interpretation explains the very gradual indicator color change since the mercapto group should act as a weak acid and thus buffer the solution at the end point. Infrared evidence eliminates the possibility that the acidity may result from facile hydrolysis of the methyl ester group α to a mercapto group, because neutralization of methyl 2-mercaptostearate followed by acidification gives a compound with the same spectrum as the starting material. This experiment also shows that the mercaptide salt is reconverted to the mercaptan by acid. Finally, it has been shown that methyl mercaptoacetate,^{15a} which also has an α -mercapto group, likewise neutralizes a nearly equimolar amount of sodium hydroxide under the foregoing titration conditions.

Although the methyl esters are acidic when they have an α -mercapto group, the mercapto group does not titrate as an acid when it is α - to a carboxyl group. Although 2-mercaptostearic acid is titrated to the phenolphthalein end point by an equimolar amount of sodium hydroxide, the product is sodium 2-mercaptostearate rather than the sodium mercaptide. This is shown by the infrared spectrum of the sodium salt, which has the carboxylate ion bands and no carboxyl group bands.

The difference in neutralization behavior between α -mercapto esters and α -mercapto acids may be explained as follows. The positive dipole on the carbonyl group of the methyl ester exerts sufficient electron pull (or proton repulsion) making the mercapto group more acidic. The mercapto

(14) R. T. O'Connor, C. H. Mack, E. F. DuPré, and W. G. Bickford, *J. Org. Chem.*, **18**, 693 (1951).

(14a) L. Pauling, *The Nature of the Chemical Bond*, 2nd ed., Cornell University Press, Ithaca, N. Y., 1940, p. 329.

(15) D. Plant, D. S. Tarbell, and C. Whiteman, *J. Am. Chem. Soc.*, **77**, 1572 (1955).

(15a) $pK_a = 7.8$ in $0.15N$ NaCl, 25° , reported by M. Calvin in *Glutathione*, Academic Press, N. Y., 1954, p. 9.

group in the α -mercapto acids is, however, less acidic than the carboxyl group. Formation of a carboxylate ion makes the mercapto group less acidic because the negative charge of this ion decreases the positive dipole which tends to dissociate the mercapto group proton in the ester. Furthermore, the product from the neutralization of both the mercapto and carboxyl groups would be a dianion whose formation would be minimized because of the coulombic repulsion of the neighboring negative groups.

Ultraviolet spectra. Further evidence of interaction of the carbomethoxy group with sulfur in the α -position is given by the ultraviolet absorption spectra of the disulfide dimethyl esters. Dimethyl 9(10),9'(10')-dithiodistearate has an absorption maximum at 247 $m\mu$ and $\log \epsilon = 2.62$ (Fig. 2A),

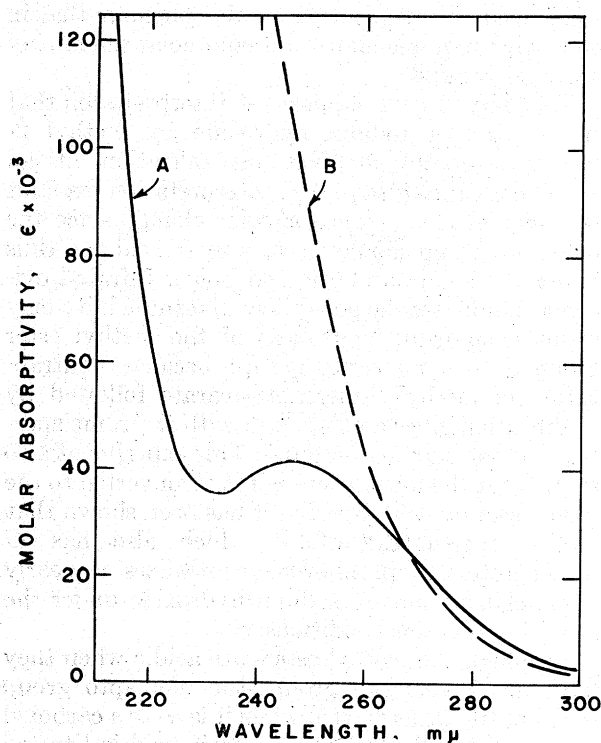


Fig. 2. Ultraviolet absorption spectra of disulfides: (A) Dimethyl 9(10),9'(10')-dithiodistearate and (B) Dimethyl 2,2'-dithiodistearate

and is thus similar to alkyl disulfides.¹⁶ In dimethyl 2,2'-dithiodistearate the sulfur atoms are in the α -position to the ester groups. The effect of this proximity is a continuous absorption increasing toward the short wave length region (Fig. 2B). The generality of this phenomenon is shown by spectra on two other compounds. Dimethyl 11,11'-dithiodiundecanoate, in which the disulfide group is far removed from the ester groups, has an absorption curve similar to that of dimethyl 9(10),9'(10')-dithiodistearate and a maximum at 250

$m\mu$. On the other hand, dimethyl 2,2'-dithiodiacetate, in which the disulfide and ester groups are separated by only one carbon atom, has a continuous absorption curve nearly identical to that of dimethyl 2,2'-dithiodistearate. It has been reported recently¹⁷ that similar effects are shown by some disulfide dicarboxylic acids and their sodium salts.

EXPERIMENTAL

Starting materials and reference compounds. Thiolacetic acid was purified by fractional distillation of the best commercial grade. Methyl 2-hydroxystearate, m.p. 63–65°, was prepared from 2-hydroxystearic acid.¹⁸ Methyl 12-hydroxystearate, m.p. 56–58°, was prepared by methanolysis of fully hydrogenated castor oil followed by three crystallizations from acetone at 15°. Methyl oleate was prepared from methyl esters of olive oil by multiple fractional distillation and low temperature crystallization.¹⁹ Dimethyl 2,2'-dithiodiacetate, n_D^{25} 1.5090, was prepared from methyl mercaptoacetate by oxidation with iodine in ethanol solution, followed by extraction with ether. Methyl mercaptoacetate was Eastman White Label Grade.

Methyl 9(10)-(acetylthio)stearate. A mixture of methyl oleate (115 g., 0.39 mole) and freshly-distilled thiolacetic acid (59 g., 0.77 mole) was irradiated in a quartz flask by a high pressure quartz mercury arc for 24 hr. at 70°. The reaction mixture was distilled under diminished pressure; yield, 115 g. (70%), n_D^{25} 1.4666, b.p. 191° at 0.8 mm.

Anal. Calcd. for $C_{21}H_{40}O_2S$: C, 67.7; H, 10.8; S, 8.61. Found: C, 67.7; H, 10.8; S, 8.56.

In accordance with its branched structure, this compound does not form a complex with urea. The urea complexing technique has been used to remove unreacted linear methyl oleate in crude reaction products.

The infrared spectrum of a liquid film shows clearly resolved ester carbonyl (1740 cm^{-1}) and thiocarbonyl (1690 cm^{-1}) bands of equal intensity. Characteristic bands of long-chain methyl esters are present. Strong bands are also present at 1115 and 950 cm^{-1} . These latter bands are also found in 11-(acetylthio)undecanoic acid and other thiolacetates.^{8,20}

Additional confirmation of the thiolacetate structure is provided by the ultraviolet absorption spectrum, which has a maximum in methanol of 232 $m\mu$ and a molar extinction coefficient of 4.4×10^3 .^{20b}

9(10)-Mercaptostearic acid. This compound has been mentioned in the literature,⁹ but it has not been well characterized. The procedure described below is an improvement over the literature method.

Methyl 9(10)-(acetylthio)stearate (11 g., 0.030 mole) was hydrolyzed by refluxing for 2 hr. in a solution of 10 g. (0.18 mole) of potassium hydroxide in 100 ml. of 50% aqueous ethanol. The solution was acidified with hydrochloric acid and extracted with ether. The ether extract was washed with water, dried over anhydrous sodium sulfate, and evaporated to give 7.7 g. (91%) of 9(10)-mercaptostearic acid as a pale yellow liquid, n_D^{25} 1.4724.

Anal. Calcd. for $C_{18}H_{36}O_2S$: C, 68.3; H, 11.5; S, 10.1; neut. equiv., 317. Found: C, 68.3; H, 11.5; S, 10.2; neut. equiv., 313.

Fractional crystallization from petroleum ether at -30°

(17) L. Schotte, *Arkiv för Kemi*, **9**, 441 (1956).

(18) P. A. Levene and P. S. Young, *J. Biol. Chem.*, **102**, 557 (1933).

(19) H. B. Knight, E. F. Jordan, Jr., E. T. Roe, and D. Swern, *Biochemical Preparations*, **2**, 100 (1952).

(20) (a) C. Knuth, A. Bavley, and W. A. Lazier, *J. Org. Chem.*, **19**, 845 (1954). (b) L. H. Noda, S. A. Kuby, and H. A. Lardy, *J. Am. Chem. Soc.*, **75**, 913 (1953).

(16) Q. W. Decker and H. W. Post, *J. Org. Chem.*, **22**, 145 (1957).

gave approximately equal precipitate and filtrate fractions with the same refractive index. These fractions were solid slightly below room temperature, but had no sharp melting point.

The infrared spectrum in carbon disulfide is very similar to that of stearic acid.¹¹

Sodium 9(10)-mercaptostearate. The sodium salt, m.p. approximately 250°, was recovered by evaporating the solution from the neutralization equivalent determination of 9(10)-mercaptostearic acid.

Anal. Calcd. for $C_{18}H_{35}O_2SNa$: S, 9.47; Na, 6.79. Found: S, 9.40; Na, 7.19.

9(10),9'(10')-Dithiodistearic acid. 9(10)-Mercaptostearic acid (3.46 g., 0.011 mole) was treated with a slight excess (101 ml.) of 0.1N iodine in ethanol, with the addition of 35 ml. of water to speed the reaction near the end point. The solution was diluted with a large amount of water and extracted with ether. The extract was dried over anhydrous sodium sulfate and evaporated to give 3.3 g. of a reddish viscous oil, n_D^{25} 1.4870.

Anal. Calcd. for $C_{36}H_{70}O_4S_2$: C, 68.6; H, 11.2; S, 10.1; neut. equiv., 316. Found: C, 69.0; H, 11.3; S, 9.21; neut. equiv., 316.

The infrared spectrum is very similar to that of 9(10)-mercaptostearic acid.

Methyl 9(10)-mercaptostearate. (a) *By esterification of 9(10)-mercaptostearic acid.* 9(10)-Mercaptostearic acid (1.24 g., 0.004 mole), 2% by weight (25 mg.) of naphthalene-2-sulfonic acid catalyst, and 10 ml. (0.25 mole) of methanol were refluxed for 6 hr. The solution was diluted with water and extracted with ether. The ether extract was washed with water, dried with anhydrous sodium sulfate and evaporated. The residual liquid, methyl 9(10)-mercaptostearate, weighed 1.01 g., n_D^{25} 1.4648.

Anal. Calcd. for $C_{19}H_{35}O_2S$: C, 69.0; H, 11.6; S, 9.70. Found: C, 69.1; H, 11.6; S, 9.62.

(b) *By alcoholysis of methyl 9(10)-(acetylthio)stearate.* Base-catalyzed alcoholysis²¹ of methyl 9(10)-(acetylthio)stearate gave the desired mercapto ester directly. Sodium (0.1 g.) was dissolved in 60 ml. (1.5 moles) of methanol. Methyl 9(10)-(acetylthio)stearate (11 g., 0.030 mole) was added, and the solution was refluxed for 4 hr. The solution was evaporated to a gel-like solid, acidified with dilute hydrochloric acid, and extracted with ether. The ether extract, after washing and drying, was evaporated to give 8.5 g. of crude product. The analytical sample, n_D^{27} 1.4638, was obtained by high-vacuum distillation in a short path still. Its infrared spectrum was the same as that of the product obtained by esterification of 9(10)-mercaptostearic acid.

Anal. Calcd. for $C_{19}H_{35}O_2S$: C, 69.0; H, 11.6; S, 9.70. Found: C, 69.0; H, 12.3; S, 9.70.

Dimethyl 9(10),9'(10')-dithiodistearate. This disulfide was prepared by titrating methyl 9(10)-mercaptostearate with iodine in ethanol as described earlier. The solution was cooled to -20° and the resulting crystalline precipitate was separated, washed with cold acetone, and dried. The product (yield about 50%) was a pale liquid, n_D^{25} 1.4790.

Anal. Calcd. for $C_{38}H_{74}O_4S_2$: C, 69.2; H, 11.3; S, 9.71. Found: C, 69.0; H, 11.1; S, 9.83.

2-Bromostearic acid. 2-Bromostearic acid was prepared by a previously reported procedure.²²

2-Mercaptostearic acid. This compound has been described previously,²³ but the procedure given below is an improvement over earlier ones. 2-Bromostearic acid (181.5 g., 0.5 mole), 38 g. (0.5 mole) of thiourea, and 1000 ml. of ethanol were refluxed for 4 hr. A solution of 220 g. of sodium hydroxide in 1200 ml. of 80% aqueous ethanol was then added and the reaction mixture was refluxed for an additional 46 hr. The cooled reaction mixture was then added to 1500 ml.

of 4N hydrochloric acid with stirring at such a rate that the temperature did not rise above 60°. After the acidification was completed, the reaction mixture was heated on a steam bath until the crude 2-mercaptostearic acid was molten and had collected on the surface of the aqueous layer. The mixture was cooled to room temperature, a hole was punched in the crude solidified 2-mercaptostearic acid, and the aqueous layer was poured off. The crude 2-mercaptostearic acid was washed free of salt and acid by melting and stirring it on a steam bath with several 500-ml. portions of water and intervening solidification as described. The crude product was air-dried and crystallized from 1300 ml. of ethanol (charcoal used); yield, 106 g., (67%) m.p. 75-78°; neut. equiv. calcd., 316.5; found, 320. Three recrystallizations of a small sample of the above product yielded analytically pure 2-mercaptostearic acid, m.p. 79-79.5° (lit. 80°); neut. equiv. 318.

The infrared spectrum of 2-mercaptostearic acid in carbon tetrachloride solution is quite similar to that of 9(10)-mercaptostearic acid except in two respects. The band at 1240 cm^{-1} is shifted to 1210 cm^{-1} . This is the region where some of the alpha mercapto ester shifts occur. In addition 2-mercaptostearic acid has a weak band at about 690 cm^{-1} .

Methyl 2-mercaptostearate. Ten grams of 2-mercaptostearic acid was refluxed for 4 hr. in 1 l. of methanol containing 3% HCl. The methanol was evaporated and the residue was extracted with ether. The extract was washed with water, dried over anhydrous sodium sulfate, and evaporated to give 9.7 g. of amber liquid, n_D^{25} 1.4621. A purified product was obtained as a colorless liquid by high vacuum distillation, b.p. 130° at 0.3 mm., n_D^{27} 1.4607.

Anal. Calcd. for $C_{18}H_{35}O_2S$: S, 9.70. Found: S, 9.74.

Dimethyl 2,2'-dithiodistearate. Methyl 2-mercaptostearate (2 g.) was titrated with 0.1N iodine in 80% ethanol until a permanent yellow color was obtained. The oil that separated from the solution was dissolved in ether. The ether extract was washed with water, dried over anhydrous sodium sulfate, and evaporated, yielding 1.5 g. of a colorless liquid, n_D^{25} 1.4749.

Anal. Calcd. for $C_{38}H_{74}O_4S_2$: C, 69.2; H, 11.3; S, 9.71. Found: C, 69.6; H, 11.4; S, 9.20.

11-Mercaptoundecanoic acid. 11-(Acetylthio)undecanoic acid⁶ (26 g., 0.10 mole) was refluxed for 3 hr. with a solution of 11.2 g. (0.20 mole) of potassium hydroxide in 100 ml. of 50% aqueous ethanol. Acidification with hydrochloric acid gave a solid, which was filtered, washed with water, and dried; yield, 20.1 g. (92%); m.p. 45°. An analytical sample, m.p. 49-51°, was obtained by low temperature crystallization from petroleum ether.

The infrared spectrum, run on a pressed potassium bromide disk, resembles that of a typical long-chain unsubstituted acid. The band progression region showed six bands, excluding the 1300 cm^{-1} carboxyl band, in accordance with studies of other terminally substituted sulfur-containing undecanoic acids.¹²

11,11'-Dithiodiundecanoic acid. 11-Mercaptoundecanoic acid was further characterized by oxidation with iodine to the known disulfide, m.p. 93° (lit.²³ 92°). The ultraviolet spectrum of the disulfide in methanol showed the expected maximum at 240 m μ , log ϵ = 2.61.

Methyl 11-mercaptoundecanoate. 11-Mercaptoundecanoic acid was esterified with methanol by the procedure used in preparing methyl 9(10)-mercaptostearate. The ester was purified by crystallization at -20° from methanol, followed by vacuum distillation. It was a colorless liquid, n_D^{24} 1.4641, that froze at or above 2°.

Anal. Calcd. for $C_{17}H_{34}O_2S$: C, 62.0; H, 10.4; S, 13.8. Found: C, 62.2; H, 10.4; S, 13.1.

The infrared spectrum had the normal long-chain methyl ester triplet. It was similar to that of methyl 9(10)-mercaptostearate except that its lower molecular weight resulted in

(21) G. S. Sasin, P. R. Schaeffer, and R. Sasin, *J. Org. Chem.*, **22**, 1183 (1957).

(22) R. S. Sweet and F. L. Estes, *J. Org. Chem.*, **21**, 1426 (1956).

(23) A. Cohen, *J. Chem. Soc.*, 593 (1932).

somewhat stronger bands at 2560 cm^{-1} (mercapto group) and 1440 cm^{-1} (carbomethoxy group).

Dimethyl 11,11'-dithiodiundecanoate. When the ethanol solution from the iodine titration of methyl 11-mercapto-undecanoate was cooled to 0° , a crystalline precipitate formed. This solid crystallized from petroleum ether as transparent plates, m.p. 56° .

Anal. Calcd. for $\text{C}_{24}\text{H}_{46}\text{O}_4\text{S}_2$: C, 62.3; H, 10.0; S, 13.9. Found: C, 62.7; H, 10.1; S, 13.7.

Analytical and physical data. The mercapto compounds described in this paper were analyzed by titration with $0.1N$ iodine in ethanol. Water was added during the titration in case of slow decolorization as the end point was approached.

With mercapto acids, the sample was first titrated in ethanol with $0.1N$ aqueous sodium hydroxide to the phenolphthalein end point. Following this determination of the carboxyl group, the pink color was just discharged with a few drops of $0.1N$ hydrochloric acid and the solution was then titrated with $0.1N$ iodine in ethanol to a faint permanent yellow color. The solution was titrated once again with $0.1N$ sodium hydroxide solution until the yellow color began to turn pink. The latter titration measured hydriodic acid liberated by the reaction of iodine with the mercapto

group, and checked on possible impurities that merely absorbed iodine. With pure mercapto acids analysis showed equivalent amounts of carboxyl and mercapto groups and liberated hydriodic acid.

Infrared absorption spectra were obtained on thin liquid films or on carbon disulfide solutions with a Perkin-Elmer Model 21 spectrophotometer, using sodium chloride optics. In a few instances, solid compounds were examined as pressed potassium bromide disks or as nujol mulls. Ultraviolet absorption spectra were recorded on methanol solutions with a Carey Model 11 recording spectrophotometer.

Acknowledgment. The carbon, hydrogen, and sulfur analyses were carried out by C. L. Ogg and associates and by Huffman Microanalytical Laboratories. Carl T. Leander, Jr., and Anne M. Smith obtained the infrared and ultraviolet spectra, respectively. The authors thank John S. Showell for helpful discussions.

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